## **EAST Search History**

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	4	"736739".ap.	US-PGPUB; USPAT	OR	ON	2007/03/05 12:58
L2	608	564/163.ccls.	US-PGPUB; USPAT	OR	ON	2007/03/05 12:59
L3	317	562/504.ccls.	US-PGPUB; USPAT	OR	ON	2007/03/05 12:59
L4	1388	514/563.ccls.	US-PGPUB; USPAT	OR ·	ON	2007/03/05 12:59
L5	9	L3 and L4	US-PGPUB; USPAT	OR	ON .	2007/03/05 12:59
L6	0	L5 and 12	US-PGPUB; USPAT	OR	ON	2007/03/05 12:59
L7	0	L3 and I2	US-PGPUB; USPAT	OR	ON	2007/03/05 13:00
L8	158	549/83.ccls.	US-PGPUB; USPAT	OR·	ON	2007/03/05 13:00
L9	550	549/72.ccls.	US-PGPUB; USPAT	OR	ON	2007/03/05 13:00
L10	1	l8 and l9	US-PGPUB; USPAT	OR	ON	2007/03/05 13:00
L11	379	549/71.ccls.	US-PGPUB; USPAT	OR	ON	2007/03/05 13:01
L12	3	l11 and l8	US-PGPUB; USPAT	OR	ON	2007/03/05 13:01
S1	6	"736711".ap.	US-PGPUB; USPAT	OR	ON	2006/10/10 10:21
S2	102	562/603.ccls.	US-PGPUB; USPAT	OR	ON	2006/04/24 09:03
S3	0	562/604.6.ccls.	US-PGPUB; USPAT	OR ·	ON	2006/04/24 09:01
S4	0	562/504.6.ccls.	US-PGPUB; USPAT	OR	ON	2006/04/24 09:02
S5	312	562/504.ccls.	US-PGPUB; USPAT	OR	ON	2006/04/24 09:02
S6	126	562/622.ccls.	US-PGPUB; USPAT	OR	ON	2006/04/24 09:02
S7	1	S2 and S5	US-PGPUB; USPAT	OR	ON	2006/04/24 09:03
S8	0	S2 and S6	US-PGPUB; USPAT	OR	ON	2006/04/24 09:03
S9	1250	514/563.ccls.	US-PGPUB; USPAT	OR	ON	2006/04/24 09:03

## **EAST Search History**

S10	0	S2 and S9	US-PGPUB; USPAT	OR	ON	2006/04/24 09:04
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S12	3	S6 and S9	US-PGPUB; USPAT	OR	ON	2006/04/24 09:04
S13	1	"7071355".pn.	US-PGPUB; USPAT	OR	ON	2006/10/09 06:57
S14	0	"736739".pn.	US-PGPUB; USPAT	OR	ON	2006/10/09 06:57
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S17	1	"7071355".pn.	US-PGPUB; USPAT	OR	ON	2006/10/10 10:21

10736,739B Yong Chu 3-5-2007

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                has been enhanced and reloaded
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     5 NOV 03 JAPIO enhanced with IPC 8 features and functionality
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NEWS 6 NOV 10 CA/CAplus F-Term thesaurus enhanced
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NEWS
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        NOV 20
                to 50,000
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NEWS 9
NEWS 10 DEC 11 CAS REGISTRY chemical nomenclature enhanced
NEWS 11 DEC 14 WPIDS/WPINDEX/WPIX manual codes updated
NEWS 12 DEC 14 GBFULL and FRFULL enhanced with IPC 8 features and
                functionality
NEWS 13 DEC 18 CA/Caplus pre-1967 chemical substance index entries enhanced
                with preparation role
                CA/CAplus patent kind codes updated
NEWS 14
        DEC 18
NEWS 15 DEC 18
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                to 50,000
NEWS 16 DEC 18 MEDLINE updated in preparation for 2007 reload
NEWS 17 DEC 27
                CA/CAplus enhanced with more pre-1907 records
NEWS 18 JAN 08 CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 19 JAN 16 CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 20 JAN 16
                IPC version 2007.01 thesaurus available on STN
NEWS 21 JAN 16 WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 22 JAN 22 CA/CAplus updated with revised CAS roles
NEWS 23 JAN 22
                CA/CAplus enhanced with patent applications from India
NEWS 24 JAN 29
                PHAR reloaded with new search and display fields
                CAS Registry Number crossover limit increased to 300,000 in
NEWS 25 JAN 29
                multiple databases
NEWS 26 FEB 13
                CASREACT coverage to be extended
NEWS 27 Feb 15 PATDPASPC enhanced with Drug Approval numbers
NEWS 28 Feb 15 RUSSIAPAT enhanced with pre-1994 records
NEWS 29 Feb 23 KOREAPAT enhanced with IPC 8 features and functionality
NEWS 30 Feb 26 MEDLINE reloaded with enhancements
NEWS 31 Feb 26 EMBASE enhanced with Clinical Trial Number field
NEWS 32 Feb 26 TOXCENTER enhanced with reloaded MEDLINE
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NEWS 33 Feb 26 IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 34 Feb 26 CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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FULL ESTIMATED COST

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chain nodes :

6 7 20 21 22 23 24 25 27 29 32 34 36

ring nodes :

1 2 3 4 5 8 9 10 11 12 13 14 15 16 17 18 19

chain bonds :

1-29 3-27 4-23 5-6 6-7 6-22 7-8 7-32 11-14 16-20 20-21 23-24 23-25 25-36

ring bonds :

1-2 1-5 2-3 3-4 4-5 8-9 8-13 9-10 10-11 11-12 12-13 14-15 14-19 15-16

16-17 17-18 18-19

exact/norm bonds :

1-2 1-5 1-29 2-3 3-4 3-27 4-5 4-23 5-6 6-7 6-22 7-8 7-32 11-14 16-20

20-21 23-24 23-25 25-36

normalized bonds :

8-9 8-13 9-10 10-11 11-12 12-13 14-15 14-19 15-16 16-17 17-18 18-19

G1:C,S

G2:H,OH,CH3

G3:H,CH3

G4: CH3, CH2, CF3

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:Atom 9:Atom 10:Atom

11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom

20:CLASS 21:CLASS

22:CLASS 23:CLASS 24:CLASS 25:CLASS 27:CLASS 29:CLASS 32:CLASS 34:CLASS

## L1 STRUCTURE UPLOADED

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L1 HAS NO ANSWERS

L1 STR

$$G_2$$
 $G_3$ 
 $G_4$ 
 $G_2$ 
 $G_3$ 
 $G_4$ 
 $G_2$ 
 $G_3$ 

G1. C, S

G2 H,OH,Me

G3 H,Me

G4 Me, CH2, CF3

Structure attributes must be viewed using STN Express query preparation.

2 ANSWERS

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SAMPLE SEARCH INITIATED 11:01:29 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 2 TO ITERATE

100.0% PROCESSED 2 ITERATIONS SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 2 TO 124

PROJECTED ANSWERS: 2 TO 124

L2 2 SEA SSS SAM L1

=> s ll full

FULL SEARCH INITIATED 11:01:36 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 90 TO ITERATE

100.0% PROCESSED 90 ITERATIONS 27 ANSWERS

SEARCH TIME: 00.00.01

L3 27 SEA SSS FUL L1

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L4

6 L3

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L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2006:87597 CAPLUS Full-text

DOCUMENT NUMBER:

144:304503

TITLE:

Dual Binding Mode of a Nove Series of DHODH

Inhibitors

AUTHOR(S):

Baumgartner, Roland; Walloschek, Markus; Kralik,

Martin; Gotschlich, Astrid; Tasler, Stefan; Mies, Jan;

Leban, Johann

CORPORATE SOURCE:

SOURCE:

4SC AG, Martingried, 82152, Germany

Journal of Medicinal Chemistry (2006),

1239-1247/

CODEN: MCMAR; ISSN: 0022-262

PUBLISHER:

American Chemical Society

DOCUMENT TYPE:

Journal

LANGUAGE:

English

Human dihydroorotate dehydrogenase (DHODH) represents an important target for the treatment of hyperproliferative and inflammatory diseases. In the cell DHODH catalyzes the rate-limiting step of the de novo pyrimidine biosynthesis. DHODH inhibition results in beneficial immunosuppressant and antiproliferative effects in diseases such as rheumatoid arthritis. Here, we present high-resoln. X-ray structures of human DHODH in complex with a novel class of low mol. wt. compds. that inhibit the enzyme in the nanomolar range. Some compds. showed an interesting dual binding mode within the same cocrystal strongly depending on the nature of chem. substitution. Measured in vitro activity data correlated with the prevailing mode of binding and explained the obsd. structure-activity relationship. Addnl., the X-ray data confirmed the competitive nature of the inhibitors toward the putative ubiquinone binding site and will guide structure-based design and synthesis of mols. with higher activity.

IT 669063-49-4 669063-57-4 669063-59-6

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic

use); BIOL (Biological study); USES (Uses)

(dual binding mode of novel series of DHODH inhibitors)

669063-49-4 CAPLUS RN

1-Cyclopentene-1-carboxylic acid, 2-[[[3-fluoro-3'-(trifluoromethoxy)[1,1'-CN biphenyl]-4-yl]amino]carbonyl]- (9CI) (CA INDEX NAME)

669063-57-4 CAPLUS RN

1-Cyclopentene-1-carboxylic acid, 2-[[[3,5-difluoro-3'-CN (trifluoromethoxy)[1,1'-biphenyl]-4-yl]amino]carbonyl]- (9CI) (CA INDEX NAME)

669063-59-6 CAPLUS RN

1-Cyclopentene-1-carboxylic acid, 2-[[[2,3,5,6-tetrafluoro-3'-CN (trifluoromethoxy) [1,1'-biphenyl]-4-yl]amino]carbonyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 36 SITED REFERENCES AVAILABLE RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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36

ACCESSION NUMBER: 2005:1251885 CAPLUS Full-text

DOCUMENT NUMBER:

144:150196

TITLE: .

Biphenyl-4-ylcarbamoyl thiophenecarboxylic acids as

potent DHODH inhibitors

AUTHOR (S):

Leban, Johann; Kralik, Martin; Mies, Jan; Baumgartner,

Roland; Gassen, Michael; Tasler, Stefan

4SC AG, Martinsried, 82152, Germany CORPORATE SOURCE:

SOURCE:

Bioorganic & Medicinal Chemistry Letters (2006)

16(2), 267-270

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER:

Elsevier B.V.

DOCUMENT TYPE:

Journal

LANGUAGE:

English

OTHER SOURCE(S):

CASREACT 144:150196

$$\mathbb{R}^{1}$$
 O  $\mathbb{R}$  OMe

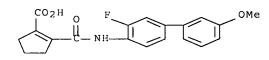
A previously discovered dihydroorotate dehydrogenase (DHODH) inhibitor series AB: was further improved by replacing the cyclopentene ring by arom. heterocycles. Different isomers of these compds., e.g. I (R1 = R2 = HO2C, R3 = H; R1 = R3 = HO2C, R2 = H; R1 = H, R2 = R3 = HO2C), were prepd. by the directed orthometalation procedure. The compds. are more active than the corresponding cyclopentene analogs and show potent effects on periferal blood mononuclear cell (PBMC) proliferation.

IT 717824-30-1

> RL: PAC (Pharmacological activity); BIOL (Biological study) (prepn. and biol. evaluation of biphenylcarbamoyl thiophene- and furancarboxylic acids as dihydroorotate dehydrogenase inhibitors and periferal blood mononuclear cell antiproliferative agents)

717824-30-1 CAPLUS RN

1-Cyclopentene-1-carboxylic acid, 2-[[(3-fluoro-3'-methoxy[1,1'-biphenyl]-CN 4-yl)amino]carbonyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 3 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

7

ACCESSION NUMBER:

2005:1024942 CAPLUS Full-text

DOCUMENT NUMBER:

143:398883

TITLE:

SAR, species specificity, and cellular activity of

cyclopentene dicarboxylic acid amides as DHODH

AUTHOR (S):

Leban, Johann; Kralik, Martin; Mies, Jan; Gassen,

Michael; Tentschert, Karin; Baumgartner, Roland

CORPORATE SOURCE:

4SC AG, Martinsried, 82152, Germany

SOURCE:

Bioorganic & Medioinal Chemistry Letters (2005)

15(21), 4854-4857

CODEN: BMCLES; ISSN: 0960-894X

PUBLISHER:

DOCUMENT TYPE:

Elsevier B.V.

Journal

LANGUAGE:

English

OTHER SOURCE(S): CASREACT 143:398883

AB Novel DHODH inhibitors were developed based on a previously described series by introduction of heteroatoms into the cyclopentene ring and hydroxyl groups attached to it. Also, the hydrophobic biphenyl side chain was replaced with benzyloxy Ph groups. Activities on human, rat, and mouse enzymes indicate a species specificity of these inhibitors.

IT 717824-30-1P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(cyclopentene dicarboxylic acid amides as DHODH inhibitors)

RN · 717824-30-1 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[[(3-fluoro-3'-methoxy[1,1'-biphenyl]-4-yl)amino]carbonyl]- (9CI) (CA INDEX NAME)

IT 669063-57-4P 669063-59-6P 717824-35-6P

717824-36-7P 867287-88-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(cyclopentene dicarboxylic acid amides as DHODH inhibitors)

RN 669063-57-4 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[[[3,5-difluoro-3'-(trifluoromethoxy)[1,1'-biphenyl]-4-yl]amino]carbonyl]- (9CI) (CA INDEX NAME)

$$CO_2H$$
  $O$   $F$   $O-CF_3$ 

RN 669063-59-6 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[[[2,3,5,6-tetrafluoro-3'-(trifluoromethoxy)[1,1'-biphenyl]-4-yl]amino]carbonyl]- (9CI) (CA INDEX NAME)

RN 717824-35-6 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[[(3-fluoro-3'-methoxy[1,1'-biphenyl]-4-yl)amino]carbonyl]-3-hydroxy- (9CI) (CA INDEX NAME)

RN 717824-36-7 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[[(3-fluoro-3'-methoxy[1,1'-biphenyl]-4-yl)amino]carbonyl]-5-hydroxy- (9CI) (CA INDEX NAME)

RN 867287-88-5 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[[(3,5-difluoro-3'-methoxy[1,1'-biphenyl]-4-yl)amino]carbonyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2004:550931 CAPLUS Full-text

DOCUMENT NUMBER:

141:99739

TITLE:

Dihydroorotate dehydrogenase (DHODH) inhibitors and

method for their identification

INVENTOR(S):

Leban, Johann; Kramer, Bernd; Baumgartner, Roland;

Aulinger-Fuchs, Katharina; Tasler, Stefan

PATENT ASSIGNEE(S):

4SC A.-G., Germany

SOURCE:

PCT Int. Appl., 357 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

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WO 2004056747
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                         MARPAT 141:99739
OTHER SOURCE(S):
     The present invention relates to compds. contg. non-arom. ring systems or
     heteroarom. ring systems, which are capable of binding to the ubiquinone
     binding site of DHODH. Methods for identification of such compds. are also
     disclosed.
     669063-49-4D, complexes with dihydroorotate dehydrogenase
IT
     669063-57-4D, complexes with dihydroorotate dehydrogenase
     669063-59-6D, complexes with dihydroorotate dehydrogenase
    717824-30-1D, complexes with dihydroorotate dehydrogenase
     717824-33-4D, complexes with dihydroorotate dehydrogenase
     717824-34-5D, complexes with dihydroorotate dehydrogenase
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    RL: PRP (Properties)
        (dihydroorotate dehydrogenase inhibitors and inhibitor identification
        method)
RN
    669063-49-4 CAPLUS
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1-Cyclopentene-1-carboxylic acid, 2-[[[3-fluoro-3'-(trifluoromethoxy)[1,1'-

(CA INDEX NAME)

biphenyl]-4-yl]amino]carbonyl]- (9CI)

CN

RN 669063-57-4 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[[[3,5-difluoro-3'-(trifluoromethoxy)[1,1'-biphenyl]-4-yl]amino]carbonyl]- (9CI) (CA INDEX NAME)

RN 669063-59-6 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[[[2,3,5,6-tetrafluoro-3'-(trifluoromethoxy)[1,1'-biphenyl]-4-yl]amino]carbonyl]- (9CI) (CA INDEX NAME)

RN 717824-30-1 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[[(3-fluoro-3'-methoxy[1,1'-biphenyl]-4-yl)amino]carbonyl]- (9CI) (CA INDEX NAME)

RN 717824-33-4 CAPLUS

CN 2-Cyclopentene-1-carboxylic acid, 2-[[[3-fluoro-3'-(trifluoromethoxy)[1,1'-biphenyl]-4-yl]amino]carbonyl]- (9CI) (CA INDEX NAME)

CN Cyclopentanecarboxylic acid, 2-[[(3-fluoro-3'-methoxy[1,1'-biphenyl]-4-yl)amino]carbonyl]- (9CI) (CA INDEX NAME)

RN 717824-35-6 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[[(3-fluoro-3'-methoxy[1,1'-biphenyl]-4-yl)amino]carbonyl]-3-hydroxy- (9CI) (CA INDEX NAME)

RN 717824-36-7 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[[(3-fluoro-3'-methoxy[1,1'-biphenyl]-4-yl)amino]carbonyl]-5-hydroxy- (9CI) (CA INDEX NAME)

RN 717824-53-8 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 3-cyano-2-[[(3-fluoro-3'-methoxy[1,1'-biphenyl]-4-yl)amino]carbonyl]-5-hydroxy- (9CI) (CA INDEX NAME)

RN 717824-54-9 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[[[3-fluoro-3'-(trifluoromethoxy)[1,1'-biphenyl]-4-yl]amino]carbonyl]-3-hydroxy-5-sulfo- (9CI) (CA INDEX NAME)

RN 717824-57-2 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 3-cyano-2-[[(3-fluoro-3'-methoxy[1,1'-biphenyl]-4-yl)amino]carbonyl]-5-(1H-tetrazol-5-yl)- (9CI) (CA INDEX NAME)

RN 717824-60-7 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[[[3-fluoro-3'-(trifluoromethoxy)[1,1'-biphenyl]-4-yl]amino]carbonyl]-3,5-dihydroxy- (9CI) (CA INDEX NAME)

RN 717824-64-1 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 3-cyano-2-[[[3-fluoro-3'-(trifluoromethoxy)[1,1'-biphenyl]-4-yl]amino]carbonyl]- (9CI) (CA INDEX NAME)

RN 717824-86-7 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[[(3-fluoro-3'-methoxy[1,1'-biphenyl]-4-yl)amino]carbonyl]-3-hydroxy-5-nitro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{CO}_2\text{H} & \text{O} & \text{F} \\ \text{O}_2\text{N} & \text{O}_{\text{H}} & \text{O}_{\text{Me}} \end{array}$$

RN 717825-01-9 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 3-cyano-2-[[(3-fluoro-3'-methoxy[1,1'-biphenyl]-4-yl)amino]carbonyl]-5-nitro- (9CI) (CA INDEX NAME)

RN 717825-16-6 CAPLUS

CN 2-Cyclopentene-1,2-dicarboxylic acid, 3-[[(3-fluoro-3'-methoxy[1,1'-biphenyl]-4-yl)amino]carbonyl]-4-hydroxy- (9CI) (CA INDEX NAME)

$$HO_2C$$
 $OH$ 
 $OH$ 
 $OH$ 
 $OH$ 

RN 717825-40-6 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[[(3-fluoro-3'-methoxy[1,1'-biphenyl]-4-yl)amino]carbonyl]-3,5-dihydroxy- (9CI) (CA INDEX NAME)

RN 717825-46-2 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[[[3,5-difluoro-3'-(trifluoromethoxy)[1,1'-biphenyl]-4-yl]amino]carbonyl]-3-hydroxy-5-nitro-(9CI) (CA INDEX NAME)

$$O_2N$$
 $O_1$ 
 $O_2$ 
 $O_3$ 
 $O_4$ 
 $O_4$ 
 $O_5$ 
 $O_5$ 
 $O_7$ 
 $O_7$ 

REFERENCE COUNT:

THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

10

ACCESSION NUMBER:

2004:550930 CAPLUS Full-text

DOCUMENT NUMBER:

141:106198

TITLE:

A preparation of cycloalkenedicarboxylic acid

derivatives, useful as dihydroorotate dehydrogenase

APPLICATION NO.

WO 2003-EP14434 W 20031217

DATE

(DHODH) inhibitors

INVENTOR (S):

Leban, Johann; Kralik, Martin

PATENT ASSIGNEE(S):

4SC A.-G., Germany

DATE

SOURCE:

PCT Int. Appl., 56 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

KIND

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.

	WO	2004	05674	16		A1 20040708			WO 2003-EP14434					20031217					
	,	W :	ΑE,	AG,	AL,	AM,	AT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,	
			CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	
			GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	ΚP,	KR,	KΖ,	LC,	LK,	LR,	
			LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,	
			PL,	PT,	RO,	RU,	SD,	SE,	SG,	SK,	SL,	TJ,	TM,	TN,	TR,	TT,	TZ,	UA,	
`	)		•		•		•	,	ZM,										
	/	RW:	BW,	GH,	GM,	KE,	LS,	MW,	ΜZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	
ノノ			BY,	KG,	KΖ,	MD,	RU,	TJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	
			ES,	FI,	FR,	GB,	GR.,	HU,	IE,	IT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	
			TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG
	CA	2509	138			Al	;	2004	0708		CA 2	2003-	2509	138		2	0031	217	
	ΑU	2003	2993	16		Al	;	2004	0714	•	AU 2	2003-	2993	16		2	0031	217	
. \	US	2004	17645	58		A1	;	2004	0909		US 2	2003-	7367.	11		2	0031	217	
	US	7071	355		•	В2		2006	0704										
	US	2004	19275	58		A1		2004	0930		US 2	2003-	7367	42		2	0031	217	
	ΕP	1581	477		•	A1		2005	1005		EP 2	2003 -	7994	87		2	0031	217	
		R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,	
			IE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR,	BG,	CZ,	EE,	HU,	SK		
	BR	2003	01773	31		A	;	2005	1122		BR 2	2003-	1773	1		2	0031	217	PX
	CN	1732	163			A	:	2006	0208		CN 2	2003-	8010	7354		2	0031	217_	wrey
	CN	1732	147			Α	:	2006	0208		CŅ 2	2003-	8010	7355		_2	0031	217	4 0
	JP	2006	51156	54		T		2006	0406		JP 2	2004 -	5613	32	/	<sup>2</sup>	0031	217	ann)
	US	2007	02719	93		A1		2007	0201		US 2	2004 -	7367.	39 <b>-</b>	•	2	0041	110	17
	ZA	2005	00438	37		Α		2006	0222		ZA 2	2005-	4387			2	0050	530	
	IN	2005	MN008	316		Α		2005	1111		IN 2	2005-1	MN81	6		2	0050	722	
PRIOR	ZTI S	APP	LN.	INFO	. :						DE 2	2002-	1026	0800	ž	A 2	0021	223	
											US 2	2002-	4352	58P		P 2	0021	223	
											US 2	2002-	4352	85P	1	P 2	0021	223	
											US 2	2003-	5269	92P		P 2	0031	205	

$$\begin{array}{c|c}
 & \mathbb{Z}^{2} & \mathbb{R}^{1} \\
\hline
 & \mathbb{R}^{2}
\end{array}$$

$$\begin{array}{c|c}
 & \mathbb{R}^{2} \\
\end{array}$$

$$\begin{array}{c|c}
 & \mathbb{R}^{2}
\end{array}$$

$$\begin{array}{c|c}
OH & O & F \\
\hline
N & F \\
\hline
CO_2H & F
\end{array}$$

AΒ The invention relates to a prepn. of cycloalkenedicarboxylic acid derivs. of formula I [wherein: A is a non-arom. ring contq. 4 to 8 carbon atoms, wherein the ring system comprises at least one double bond and wherein one or more of the carbon atoms in the ring can be replaced by S, O, N, or S(O), etc.; D is O, S, SO2, or CH2, etc.; Z1 and Z2 are independently selected from O, S, or NH, etc.; R1 is H or alkyl; R2 is H, OH, O-(cyclo)alkyl, or NH2, etc.; R3 is H, (cyclo)alkyl, aryl, alkoxy, halogen, or O-aryl, etc.; E is an alkyl or cycloalkyl group or a (mono/poly)cyclic (un)substituted ring system; Y is H, halogen, haloalkyl, haloalkyloxy, alkyl, cycloalkyl, a monocyclic or polycyclic (un) substituted ring system; n is 0 or 1], useful as antiinflammatory, immunomodulatory and antiproliferatory agents. The obtained compds. were screened in inhibition assay for dihydroorotate dehydrogenase (DHODH) activity. For instance, cyclopentenecarboxylic acid deriv. II showed IC50 value (human DHODH) of < 1.mu.M.

TT 717824-35-6P 717824-36-7P 719301-48-1P 719301-49-2P 719301-50-5P 719301-52-7P 719301-53-8P 719301-54-9P 719301-55-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of cycloalkenedicarboxylic acid derivs., useful as
antiinflammatory, immunomodulatory and antiproliferatory agents)

RN 717824-35-6 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[[(3-fluoro-3'-methoxy[1,1'-biphenyl]-4-yl)amino]carbonyl]-3-hydroxy- (9CI) (CA INDEX NAME)

RN 717824-36-7 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[[(3-fluoro-3'-methoxy[1,1'-biphenyl]-4-yl)amino]carbonyl]-5-hydroxy- (9CI) (CA INDEX NAME)

RN 719301-48-1 CAPLUS

CN 2-Cyclopentene-1,2-dicarboxylic acid, 3-[[(3-fluoro-3'-methoxy[1,1'-biphenyl]-4-yl)amino]carbonyl]- (9CI) (CA INDEX NAME)

RN 719301-49-2 CAPLUS

CN 1-Cyclopentene-1,3-dicarboxylic acid, 2-[[(3-fluoro-3'-methoxy[1,1'-biphenyl]-4-yl)amino]carbonyl]- (9CI) (CA INDEX NAME)

RN 719301-50-5 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[[(3-fluoro-3'-methoxy[1,1'-biphenyl]-4-yl)amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 719301-52-7 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 3-hydroxy-2-[[[2,3,5,6-tetrafluoro-3'-(trifluoromethoxy)[1,1'-biphenyl]-4-yl]amino]carbonyl]- (9CI) (CA INDEX NAME)

RN 719301-53-8 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 5-hydroxy-2-[[[2,3,5,6-tetrafluoro-3'-(trifluoromethoxy)[1,1'-biphenyl]-4-yl]amino]carbonyl]- (9CI) (CA INDEX NAME)

RN 719301-54-9 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[[(3'-ethoxy-3,5-difluoro[1,1'-biphenyl]-4-yl)amino]carbonyl]-3-hydroxy- (9CI) (CA INDEX NAME)

RN 719301-55-0 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[[(3'-ethoxy-3,5-difluoro[1,1'-biphenyl]-4-yl)amino]carbonyl]-5-hydroxy- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2003:981447 CAPLUS Full-text DOCUMENT NUMBER:

140:246103

TITLE:

Discovery of a novel series of DHODH inhibitors by a

docking procedure and QSAR refinement

AUTHOR(S):

Leban, Johann; Saeb, Wael; Garcia, Gabriel;

Baumgartner, Roland; Kramer, Bernd

CORPORATE SOURCE:

Martinsried, 82152, Germany

SOURCE:

Bioorganic & Medicinal Chemistry Letters (2004)

14(1), 55-58

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER:

Elsevier Science B.V.

DOCUMENT TYPE:

Journal

LANGUAGE:

English

OTHER SOURCE(S):

CASREACT 140:246103

A novel series of DHODH (dihydroorotate dehydrogenase) inhibitors was developed based on a lead which was obtained by a docking procedure and a medicinal chem. exploration. The activity of the initial lead was improved by a QSAR method to yield low nanomolar inhibitors.

669063-49-4P 669063-57-4P 669063-59-6P IT

669063-68-7P

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(discovery of a novel series of dihydroorotate dehydrogenase inhibitors by a docking procedure and QSAR refinement)

669063-49-4 CAPLUS RN

1-Cyclopentene-1-carboxylic acid, 2-[[[3-fluoro-3'-(trifluoromethoxy)[1,1'-CN biphenyl]-4-yl]amino]carbonyl]- (9CI) (CA INDEX NAME)

RN 669063-57-4 CAPLUS

1-Cyclopentene-1-carboxylic acid, 2-[[[3,5-difluoro-3'-(trifluoromethoxy) [1,1'-biphenyl]-4-yl]amino]carbonyl]- (9CI) NAME)

669063-59-6 CAPLUS RN

1-Cyclopentene-1-carboxylic acid, 2-[[[2,3,5,6-tetrafluoro-3'-CN (trifluoromethoxy)[1,1'-biphenyl]-4-yl]amino]carbonyl]- (9CI) NAME)

RN 669063-68-7 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[[(3'-ethoxy-3,5-difluoro[1,1'-biphenyl]-4-yl)amino]carbonyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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---Logging off of STN---

= >

Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	32.09	207.13
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-4.68	-4.68

STN INTERNATIONAL LOGOFF AT 11:02:31 ON 05 MAR 2007